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Revisión

Nutritional screening; control of clinical undernutrition with analytical parameters

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Abstract

Objective: **To update the system for nutritional screening.**

The high prevalence of nutritional unstability that causes the Clinical Undernutrition (CU), especially within the hospitals and assisted residencies, makes it necessary to use screening tools for the constant control of undernutrition to combat it during its development.

CU is not so much due to a nutritional deficiency but to the illness and its treatments. However, the screening systems currently used are aimed at detecting an already established undernutrition rather than at detecting any nutritional risk that may be present. The metabolic changes of the nutritional status that have a trophopathic effect, can be easily and automatically detected in plasma, which allows to make the necessary changes in treatments that might be too aggressive, as well as to apply nutritional support according to each case.

The manual screening systems can detect those somatic changes typical of undernutrition only after many days or weeks, which might be too late.

Plasma albumin is a very reliable parameter for nutritional control. A lowered amount of it, due to whatever reason, is a clear sign of a possible deficit as well as of a nutritional risk suffered by the cell way before the somatic signs of undernutrition will become apparent.

A fast detection of nutritional risk, anticipating undernutrition, offers prognostic abilities, which makes screening tools based on analytic parameters the most useful, ergonomic, reliable and efficient system for nutritional screening and prognosis in the clinical practice.

Conclusion: **It is necessary to update some concepts, to leave behind old myths and to choose modern screening systems that have proven to be efficient. This is the only way achieving the dream of controlling CU among ill and vulnerable patients.**

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Key words: *Nutritional control. CONUT. Nutritional screening. Full nutritional assessment. Clinical undernutrition. Homeostasis. Interior milieu. Nutritional risk. Trophism. Trophopathy. BIG DATA.*

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CRIBADO NUTRICIONAL; CONTROL DE LA DESNUTRICIÓN CLÍNICA CON PARÁMETROS ANALÍTICOS

Resumen

Objetivo: **Actualizar el cribado nutricional.**

La alta prevalencia del desequilibrio nutricional que genera la Desnutrición Clínica (DC), especialmente en hospitales y residencias asistidas, obliga al uso de herramientas de cribado y a controlar su evolución para combatirla sobre la marcha.

La DC deriva menos de la carencia nutricional que de los efectos de la enfermedad y sus tratamientos, pero los actuales sistemas de cribado buscan más la desnutrición ya establecida que el riesgo nutricional existente.

Las alteraciones metabólicas del equilibrio nutricional que constituyen la trofopatía se pueden captar en el plasma sin demoras, automáticamente, permitiendo rectificar actitudes terapéuticas demasiado agresivas o complementarlas con el adecuado soporte nutricional.

Con los sistemas manuales de cribado, solo pasados días o semanas se evidenciarán, tardíamente, los cambios somáticos expresivos de esa desnutrición.

La concentración de la albúmina plasmática es un parámetro muy valioso en el control nutricional. Su disminución, cualquiera que sea la causa, expresa un posible déficit pero también el riesgo nutricional a que se ve sometida la célula, antes de que la desnutrición se manifieste somáticamente.

La precocidad de la detección del riesgo nutricional, anticipándose a la desnutrición y su gran capacidad pronóstica hacen de las herramientas basadas en parámetros analíticos, el procedimiento más útil, ergonómico, seguro y eficiente para el cribado y pronóstico nutricional en el entorno clínico.

C*onclusión:* es hora de actualizar conceptos, deshacer mitos y optar por sistemas modernos de cribado eficientes, única manera de alcanzar el sueño de controlar la DC en nuestras poblaciones enfermas y frágiles.

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Palabras clave: *Control nutricional. CONUT. Cribado nutricional. Valoración del estado nutricional. Desnutrición Clínica. Homeostasis. Medio interno. Riesgo nutricional. Trofismo. Trofopatía. BIG DATA.*

Introduction

For the last 40 years there has been a rising awareness on the high prevalence of Undernutrition in hospital settings as well as in long-stay centres[1-9]. The economic and health costs that this implies are a main concern to which it is imperative to find a solution[10-15]. Some agreements have been settled at national, european and international levels in an attempt to control its development and to eradicate it[6,16-21]. In order to achieve these different kinds of screening models have been proposed[6,22,22b-24].

Most of these models were based on anamnesis and anthropometric parameters (NRS-2002[25], MUST[26], MNA[27,28], etc.). However, during the last years the models based on analytical parameters have been discarded[29-32] and we consider that this change constitutes a serious mistake because it slows down the process of risk detection.

Clinical Undernutrition (CU)[33] (which continues to be known as hospital undernutrition or undernutrition related to the illness) is not so much a consequence of nutritional deficiency but rather a result of the impact played by the illness and therapeutic procedures applied to cure it. As a consequence it is a clear mistake to aim at measuring only "*stricto sensu*" (primary or due to deficiency) undernutrition as is the case by means of anthropometric methods. These nutritional screening methods are usually too simplistic, as stated in the article "Clinical undernutrition in 2014"[33b] (In printing).

To begin with, we would like to emphasize the fact that we consider CU as an altered nutritional equilibrium which has been caused by the illness and its treatment, hence not a mere lack of nutrients. CU involves a series of alterations that occur in the internal milieu or internal environment (the "Milieu intérieur" of C. Bernard) and in blood plasma as a consequence of an illness, its treatment and the eventual complications which may arise from these. These alterations will cause undernutrition at the level of cells and tissues according to the degree and duration of the condition. These alterations are a direct and immediate expression of the nutritional unstability or trophopathy to which the treated patient is exposed. Any variations of this condition can be easily measured as they will immediately become apparent in plasma concentration of nutrients or through their biological markers. However, any somatic changes which may indicate the condition will only later on be detected by means of the screening tools which are generally used at present. Therefore, they will be detected only after many days or weeks, in comparison with the more valuable information that could be obtained with analytical parameters at an earlier stage.

This paper aims at showing the importance of early detection when aiming at the control of this type of undernutrition and its development during the clinical event. For this purpose, we sustain that analytical parameters are far more useful than anthropometrical ones due to their availability, objectivity, sensibility, specificity and precocity as well as easy to apply tools, very useful for epidemiological studies and controls. As a consequence of this, the nutritional screening tools that are based on these parameters are simpler as well as much more objective, practical, versatile and efficient, therefore they can, such as in control and prognostic kind of studies.

Nutritional control in the clinical practice (Early diagnosis, monitoring, prognosis)

Concepts and procedures[34]

Nutritional Control in the Clinical Practice consists of a continuous assessment of the nutritional risk and the nutritional state as a consequence of the clinical situation at every single moment.

We understand the concept of nutritional control as a process that should contemplate prevision and early detection of any changes in the nutritional status through appropriate nutritional screening. This should be repeated periodically as long as the destabilizing clinical situation exists.

Whenever any sort of risk is detected by screening, then a more thorough assessment of the nutritional status should follow in order to confirm the data and proceed accordingly[35]

Nutritional Screening is the process of identifying groups of people who are already in a situation of or at risk of developing an altered nutritional state, by means of fast and practical testing, and with the objective of being able to act as early as possible.

Full Nutritional Assessment (FNA), "is a thorough analysis of the nutritional situation of a patient by means collecting specific data from his clinical, pharmacological and nutritional history, as well as carrying out a physical examination, anthropometric measurements and lab testing", as stated by the SENPE Multidisciplinary Consensus on hospital undernutrition management in Spain[20].

There is still at present some overlap between the concepts of nutritional screening and FNA which we consider is absolutely necessary to clarify in order to avoid at all costs any mistaken overlap between both.

According to SENPE, FNA consists of a thorough exploration of the nutritional status of a particular patient. On the other hand, it defines the concept of screening as a process of identifying, in a particular population, *those individuals who already have an altered nutritional status or may be at risk of developing it*.

There are other different aspects among the two concepts such as the following: a) objectives b) procedures and c) parameters used.

a) *Objectives:* A screening system should be effective at achieving the diagnosis of not only an already established undernutrition but also detecting those situations at risk of developing it from the very beginning, that is, from the moment in which undernutrition may originate. This is the only way to prevent this condition and its consequences, hence to be able to eventually apply the most appropriate adjustments[17].
   A prompt detection of any nutritional unstability that may put homeostasis at risk will make it

possible to spot the risk posed by that particular unstability and to prevent it from developing further towards undernutrition. This approach will allow us to shed light on the original cause of it, being it either nutritional, illness related or a consequence of an aggressive therapy. Also, it could be possible to adjust the treatment not necessarily by modifying the nutritional support.

b) *Procedures:* The nutritional control procedures may have different indications and applications based on whether they are used for nutritional assessment or nutritional screening. The reason for this is that we consider that nutritional screening should be aimed at detecting and assessing risk of undernutrition. As a consequence, anthropometric methods are unable to guarantee an early detection of nutritional unstability derived of an acute condition, such as haemorrhage, lymphorragy or the immediate trophopathic caused by an aggressive therapy. Those methods are useful tools as a complement to a nutritional state assessment.

c) *Parameters:* The usefulness and capabilities of these may also vary greatly depending on whether they are used for screening or assessment purposes. This distinction will become clear later on when discussing the use of plasma albumin concentration, a marker that plays an essential role as nutritional indicator but which is often maligned. Although sometimes we may agree with those who discard this marker to achieve nutritional state assessment, we cannot but be opposed to those who justify its rejection by means of the same reasons when considering nutritional screening (such as referring to the average-long duration, alterations due to causes other than nutritional, etc).

It is important to remember that very frequently these discrepancies are a consequence of rejecting these analytical parameters as undernutrition markers when dealing with nutritional state assessment. We consider these to be highly efficient and valid when carrying out nutritional screening, as they are reliable markers of nutritional risk and prognosis[31,37,72,75-77].

Furthermore, the procedures which are nowadays generally recognized by the main Scientific Societies to be applied as screening tools can only be considered as too simplistic methods of assessment of an already established nutritional state. With these methods the main objective is to detect as soon as possible any anthropometric evidence of an already present undernutrition and its degree of development. However, they do not take into consideration the fact that by the time undernutrition becomes evident there have been a number of metabolic alterations occurring in the internal milieu which can be analytically traced by means of any changes the risk markers and their plasma concentration.

After clarifying the difference between NSA and nutritional screening we are now going to focus on the process of screening.

Nutritional screening

To begin with, it is essential to consider nutritional screening as a process that should not focus on the early diagnosis of undernutrition but, rather, it should be aimed at detecting those "individuals who already have or are at risk of developing an altered nutritional state, in order to be able to act promptly".

The group of people that we normally deal with is composed of ill or vulnerable individuals. These are also a group of patients who present the highest nutritional risk, although with different characteristics as compared to primary undernutrition (due to lack of nutrients). In most of these patients there is an altered nutritional status, a change in the physiological homeostasis, which has been a consequence of the illness and its treatment and that, if the condition persists, will eventually lead to undernutrition and all the complications derived from it. We consider it is absolutely necessary to modify the concept of nutritional screening when applied in the clinical practice, hence aiming at the early detection and quantification of those trophopathic alterations which occur before undernutrition, rather than the early detection of an already present undernutrition. We believe it is a serious mistake to wait until undernutrition will become physically evident; by then it will already be too late to carry out prompt intervention on the alterations of the nutritional state, as suggested by WHO.

It is imperative to put the focus on controlling Clinical Undernutrition Risk (we suggest that the term *clinical trophopathy* should be used for this purpose) in order to avoid putting the attention only on an already established undernutrition. If we think about the latter as a tree, hence our efforts should be aimed at getting a picture of the whole forest, including those twigs or problems which may eventually arise.

Analytical parameters

The purpose of the present paper is to make see that in hospital and medical settings as well as in assisted residencies for elderly and dependent kind of patients that require a constant control of their health condition, undernutrition screening must be able to detect any alteration in the nutritional equilibrium of the internal milieu from the beginning, which means to say since the illness starts to originate, and as long as it may persist, by means of most dynamic and efficient system possible. The latter, as will be shown below, should be based primarily on laboratory parameters and it can also be useful to apply some of the commonly used parameters which are routinely carried out through the protocols to supervise the health of these patients[36-38].

Another advantage of this is that the screening is done simultaneously and automatically during the period of assistance to the patients. Therefore, it is already integrated in the diagnostic and follow up protocols, which means that no added cost or professional effort is required, as contrasted with other methods which would need extra surveys and anthropometrical measures.

It is very well known that an illness and its treatments will eventually lead to undernutrition. It is also a fact that undernutrition will further aggravate the illness as well as promoting or causing new ones, as is the case of infections and the difficulty to treat this in the presence of undernutrition. All this determines the need of an early detection in order to stop the vicious circle that will eventually lead towards death. It can be said that considering the fact that both conditions work synergistically, those parameters that are normally altered by undernutrition, an illness or both will definitely be the most useful indicators to be used in order to achieve an early detection of nutritional risk.

Based on our experience we have not find anthropometrical parameters useful to be applied in nutritional screening during hospital stay. The most common problem was that the anthropometrical changes appeared too late. Also, anamnesis data was too subjective and difficult to obtain, especially in the case of elderly patients, as they are frequently limited to or totally unable to move, hence making the testing further complicated.

On the other hand, we have observed a high degree of sensibility offered by some analytical parameters in the clinical practice as these are capable of detecting and quickly express all the changes that had taken place during the clinical period. As a consequence we decided to select those to be applied in the basic profiles for the control of the clinical development, which we considered of use for nutritional screening. After this selection we designed a system for nutritional control (CONUT®) that became incorporated in the computer systems of the Clinical Test Labs. These would automatically set off an alert indicating the degree of nutritional risk between all the other results[31,37,50,58].

The analytical parameters selected for the control of any alterations in the nutritional equilibrium are based on any changes of the markers in plasma concentration as they are taking place, being these caused by insufficient intake or synthesis, organic fluid waste or liquid overload determined by a saline solution therapy, or the transfer of plasma albumin or other osmotic elements from intra to extra vascular areas. These changes are frequently a consequence either of an inflammatory condition, other pathologies or the use of medicine: That is, any cause of disturbances in the homeostasis[39,40].

The fact that these alterations are not only a consequence of primary undernutrition is not a justification for considering them as invalid tools. On the contrary, we believe that they are still useful for our purposes: a lowered concentration in the plasma of these elements (which play a key role in the physiology of cell nutrition) will lead to an altered nutritional equilibrium in the internal milieu. This will also play havoc on trophism (already altered due to illness or its treatment) and eventually increase undernutrition in the tissues, due to the cell having a reduced plasmatic concentration of nutritional or functional resources available from around it. This situation is likely to happen when the concentration drops below the physiological needs, regardless of which the cause of it was, therefore the cell will be unable to assimilate the nutrients that the patient receives, even those provided through parenteral nutrition.

Among the common reasons against the use of analytical parameters for nutritional screening, one of the most widely known is based on the fact that "the values of the analytical parameters can be altered by many situations other than 'nutritional related' ones", meaning that they are not caused by primary (or lacking) undernutrition[41,42].

We totally agree with this, although we consider it is essential to point out that many of these alterations of "non nutritional" origin are precisely the ones which in fact indicate an increase of nutritional risk because they also play a role in the altered trophopathy that exists in the internal milieu of the patient that is under control. It is possible indeed that these alterations may not be a consequence of undernutrition, but it is true that they may constitute the cause itself of undernutrition and its risks. Furthermore, both the cause and consequence aspects may coincide in the case of a persistent nutritional unstability.

At this point we are going to expose the reasons behind the analytical parameters that we have selected among the most widely used in the clinical practice for health control of patients with potential risk of undernutrition: Albumin, as it will be later on discussed, a reliable indicator not only of protein stores in the body, but also highly efficient as a nutrient and medical transport through the blood and lymph. Cholesterol, due to its key role in hormonal and metabolic physiology, and the fact that a decrease of it will be problematic for many areas involved in nutritional equilibrium, as well as an indirect marker of reduced caloric intake in the patient's nutrition. The same applies for total lymphocyte count: A reduction of these in plasma concentration is partly caused by insufficient calorie-protein intake. However, it can also be caused by other treatments or particular illnesses. In any case, it is still a highly useful marker of nutritional risk in elderly and ill patients, especially in those who are under aggressive treatments[50].

There is a tendency, on the one hand, to put the focus of nutritional screening at finding the type of nutritional deficiency that caused the condition and, on the other hand, to choose the best nutritional treatment to correct those deficiencies. This approach could be valid for those screening systems that are aimed at diagnosing primary undernutrition (due to lack of nutrients) but not necessarily so when the aim is to spot as well any kind of risk that may derive from a trophopathic alteration due to other reasons. Whenever we focus on analytical parameters, which are more sensitive, the solution may not always be achieved with nutritional approaches. Considering that by means of our tool we are able to detect any risk before undernutrition can develop, then it may be sufficient to make the appropriate modifications to the real causes of nutritional instability. Once the alert appears an analyses of it will follow, and if there is evidence that it has been caused by the illness, then a modification to the treatment will be performed. It could also be necessary to change the therapeutic procedure, if this shows to be the cause of the trophopathy that is putting the patient at risk. The sooner we act, the more likely we will be able to prevent undernutrition from developing and playing any havoc.

This is not to be achieved just by nutritional support but by a complex of measures aimed at improving the

treatment, that is, on the one hand, by applying nutritional support and on the other hand, by selecting those metabolically least aggressive therapies (which means to say, the least trophopathic ones) during the clinical evolution. Furthermore, the harmful effects of medication on the trophism can only be detected and measured by means of analytical parameters; this will never be possible to detect on time by means of the anthropometrical[43] and anamnesis parameters which are commonly used at present

We consider it could be reasonable to reflect on whether there is any coherence in trying to separate the nutritional aspect from the complex physiopathology that is implied in the clinical practice, that is, whether doing so can favour the process of detection, assessment and correction of an unstable nutritional equilibrium. This could only be the case whenever undernutrition has already been diagnosed, while it would pass unnoticed until that moment and during all its latent period of development.

It is important to point out that this kind of approach to screening does not mean any further uncomfort or havoc to the patient because it is based on the very same parameters that are already included in the protocols for clinical control.

Plasma albumin

We consider plasma albumin concentration is highly reliable indicator of Clinical Undernutrition because of the following reasons:

- Any variations of it during a period of illness and its treatment occur much faster than in physiological conditions.
- Whenever a decrease of it has been caused by protein intake deficiency then it has occurred as a consequence of undernutrition.
- If the decrease has been due to an illness or its treatments, then it is the cause of undernutrition and it is an indicator that the latter is under development.
- When both situations coincide a diminished albumin is to be considered as a consequence and cause of a situation characterized by nutritional risk.
- The amount and duration of the decrease is a direct indicator of nutritional risk.
- It is a highly useful prognosis indicator[44].

Those who have manifested against the use of plasma albumin for nutritional screening make reference to the possible causes that can determine a decrease of it, including the fact that "it can also be caused by non nutritionally related factors, such as liver mass function, metabolic use index, excretion of these, intra and extra vascular transfer, as well as the hydration status of the patient"[20,41].

However, these justifications do not take into account that a plasmatic decrease of protein concentration (even in the case of having a "non nutritional" origin as is the case of nutrient deficiency or primary undernutrition) are caused by what we consider a trophopathic condition. This is the one to determine a situation in which there is a functional lack in the interior milieu. As a consequence, they are the real cause of cell undernutrition.

Average albumin life-span is a common topical issue that has been frequently used to reject albumin count as a valid marker for clinical screening. This is the most serious mistake for discarding the use of this parameter in the clinical practice. It is very well known that the average life-span of plasma albumin is between 18-20 days in the case of normal adults[20,41,42]. This approximation is only valid in physiological situations. However, there are no bibliographical references regarding the average albumin life-span in pathological conditions like the ones we normally deal with.

In pathological situations and most particularly in the case of patients under aggressive treatments and in conditions of high loss or abnormal needs and fasting requirements, the aforementioned life-span can be reduced to a couple of hours. This is particularly evident in liver or serious kidney conditions as well as extravasation situations or any metabolic changes as those caused by inflammation[45], or the changes which are normally involved after surgery, and even simple causes such as can be the case of fluid therapy.

A reduction of albumin life-span during pathological conditions and during aggressive treatments make this parameter a highly efficient way to monitor any acute changes. After our many years of experience and as is constantly evident in the clinical practice, it is clear that albumin can change in a matter of just a few hours, same as cholesterol concentration and total lymphocyte count can do. This is clearly represented in the evolution graphs which are based on these parameters and that are automatically produced by the computerized methods as soon as they are detected (fig. 1). In contrast, this is completely different when dealing with anthropometrical parameters, which require some time, even several weeks or months until they will be able to detect any changes going on during the clinical period.

The idea that albumin "is a non specific marker" of undernutrition is frequently heard[36]. We do not use it as a marker of Primary Undernutrition but, on the contrary, of Clinical Undernutrition, that is of trophopathy. We consider albumin a highly specific and sensitive marker, far more useful than other parameters generally admitted and defended as valid (BMI, weight loss or approximated food intake during the previous weeks/months). It is admitted that "it is a more reliable

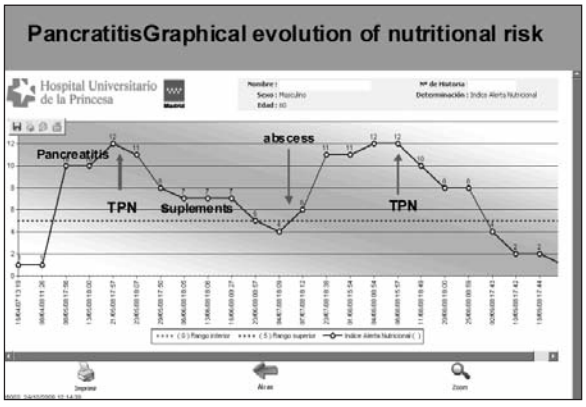

Fig. 1.—

marker than age to predict mortality and hospital stay/readmission", reason why we insist that those characteristics are precisely what make these analytical parameters highly valuable indicators of risk.

Another generalized reason against the use of albumin for nutritional screening is based on the fact that "the main problem of using it as nutritional marker is that any changes in volume as well as different pathological conditions (nephrotic syndrome, eclampsia, protein losing enteropathy, liver malfunction), and also any other type of aggression can cause a reduction of plasma albumin"[42]. In response to this idea we suggest that it is not only a good reason to justify its use as a marker of risk, but it is in fact one of the main virtues of the method when the aim is to determine the nutritional risk that has been caused and that is implied, in fact, by a reduction in its concentration. It is at that very moment when we are in a position to detect, at the most appropriate time and in the most punctual way, within the cell environment, a situation characterized by deficiency which has been caused by these or any of the other causes already mentioned, and that is resulting in undernutrition within the cell. Finally, this situation will continue as long as the detected instability persists.

Consequently, after plasma albumin has dropped, the cell will not be able to get the required nutrients that are transported by the former, including aminoacids and many others. What is more, the cell will be further deprived of any medicine that may be administered, which would otherwise be distributed by albumin, as is the case when there is a normal concentration of it in plasma. All this determines a double risk to the health of the patient that is under control.

Plasma cholesterol

As is the case for albumin, a decrease in the concentration of plasma cholesterol indicates not only a caloric deficiency but also that the cell is being deprived of an essential nutrient that is required to be able to maintain its metabolic and hormonal equilibrium (suprarenal and gonadal mainly) and to keep membrane integrity. In both cases these parameters are indicating and showing that the cell is suffering undernutrition, regardless of which the cause of this condition was[46-49].

In this regard we should mention the astonishing role played by plasma cholesterol as a trophogenic indicator over age in hospitalized patients, as illustrated in figure 3[1].

It is important to bear in mind that out of the 25.586 studied patients, almost none of them had a plasma cholesterol concentration reaching 180 mg/dl. There is an evident curve rising steadily from teenage period until 55 years of age, after which period the curve starts to lower. The decrease that takes place from the fifties can partly be caused by the use of statins, but can also be a consequence of the undernutrition that normally accompanies ageing. At present there is a generalized tendency to prescribe these drugs among this group of people (even with prophylactic purposes). This fact sustains our view that the curve change aforementioned is due to a complex of effects combined; that is Clinical Undernutrition, old age involution and (possibly as well) the use of certain medications.

Total lymphocyte count

Initially, the reason for choosing this parameter as an indicator of nutritional risk was to confirm whether a decrease of this marker could be as a consequence of protein and calorie restriction, most probably of nutritional origin, and to which the impact played by the illness and its treatment was to be added.

This was repeatedly confirmed through the many validations carried out, therefore we have been able to demonstrate the direct relationship between total lymphocyte count with the different protocols for nutritional status assessment[30,37,56]. As a consequence this marker should also be considered as a useful indicator of an increased risk of suffering any kind of infections and complications, owing to the weakened immunity involved, and regardless of which was the original cause of its reduction. Once more it is made evident that these analytical parameters are highly useful to control any situation of risk that could be present in the patient who is exposed to aggressive treatment. Hence, these parameters ease all our attempts towards the control of this condition and they even allow for immediate correction of any undesirable changes that may appear, having these been originated by the illness itself or the treatment of it.

It is to be noted that these studies did not leave out any patients suffering from hemopathy or being under aggressive treatments. This was done because in order to consider any kind of clinical risk, it was preferred to include any situation that could originate the effects that we wanted to measure.

The obtained results with this parameter did not coincide with those obtained by means of other undernutrition screening tools such as MNA, though the reasons for this are to be searched elsewhere. It is possible that those tools are unable to detect the risk indicated by lymphopenia because, as we have been able to demonstrate with the use of CONUT as screening tool in repeated occasions, it has the same expressive capacity as the other parameters which are included in it (fig. 6). In the mentioned study[50], which was carried out during a long period of time and which included all the patients whose nutritional screening at the moment of admission was available (n: 25.586), total lymphocyte concentration in plasma changed much in the same way as done by plasmatic albumin. (figs. 2 and 4).

Computer system

The obtained data can be easily handled by means of IT technology. This is another main reason for using analytical parameters as an efficient tool in the clinical practice these days. Their inevitable inclusion in the modern methodology is based on the following:

– The data in which they are based are already in IT language, from the moment that they are automatically produced by the latest Clinical Analysis Labs.

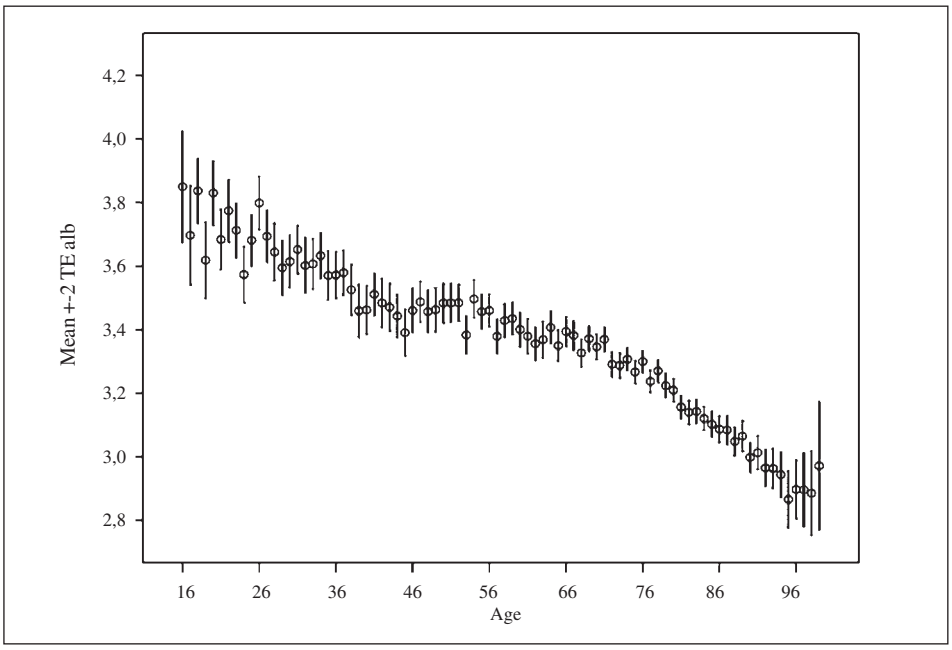

Fig. 2.—Correlation between albumina and age.

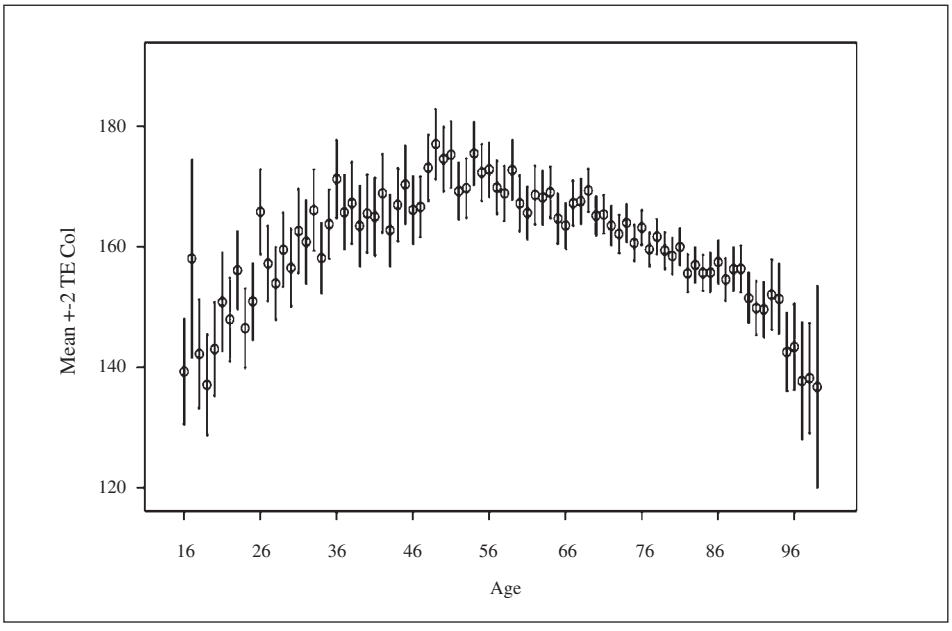

Fig. 3.—Correlation between colesterol and age.

- During the whole processing of the data, there is no risk of it being exposed to any kind of errors as a consequence of appreciation or handling.
- They are easily implemented in the already existing Computing Systems of hospitals and other assistential entities in which they are absolutely required (Primary Assistance, Convalescence Centres, Nursing Homes).
- They are very useful to carry out a wide variety of epidemiological studies in the mentioned places (BIG DATA)[51] and also a very effective tool to control the assistential quality offered by the different protocols of any area of specialty.

In this regard we already have enough data, which has been collected based on the thousands of hospitalized patients that were diagnosed with some sort of risk. This has enabled us to elaborate helpful indexes and formulas in order to predict the eventual development according to different diagnosis and therapeutical procedures, and based on the data issued by other automated methods used for the early detection of risk and Clinical Undernutrition.

Applying the methods based on artificial intelligence to this data will make it possible to determine the risk involved in each initial diagnosis, but also the different results to be obtained according to the therapeutical proce-

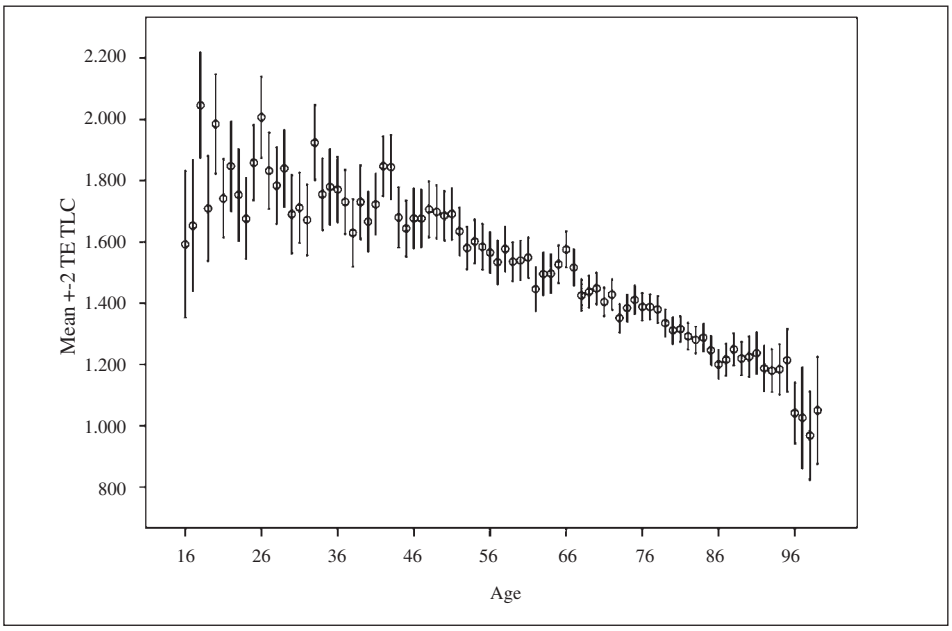

Fig. 4.—Correlation between TLC and age.

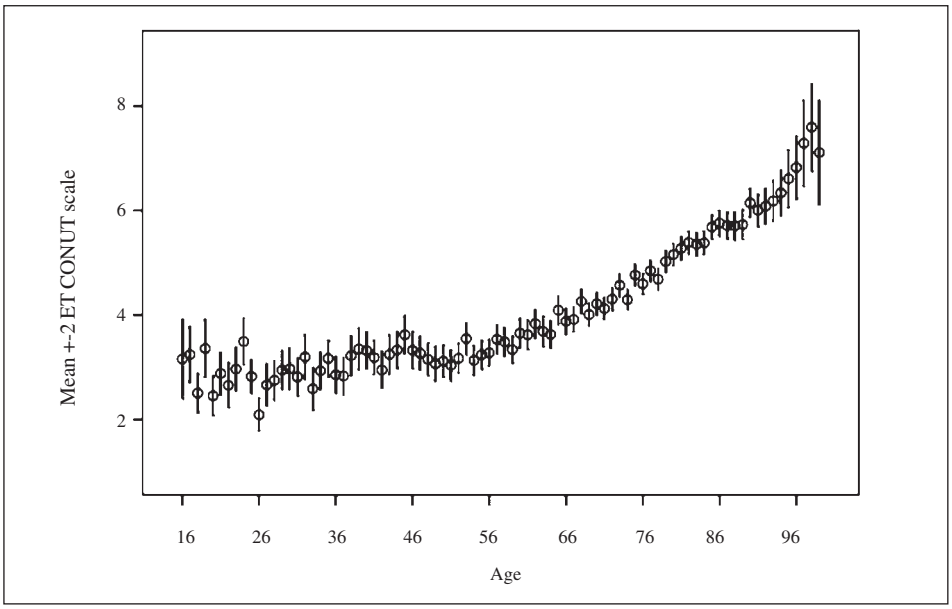

Fig. 5.—Correlation between CONUT scale and age.

dures and nutritional support applied. This will be of unquestionable help in improving the assistential quality in the future, hence at the moment of choosing the most appropriate therapeutical approach we will have different variables such as diagnosis, sex, age, therapeutical procedure and nutritional support in hand, all of which are essential to determine the risk in each particular case.

Another key advantage when applying with epidemiological purposes the data which has been obtained, processed, stored and shared through computer systems, is their easy application at a digital level with the aim of designing complex projects of control studies, many kinds such as retrospective, evolutionary, regional, national and international. By means of the rudimentary screening systems suggested at present, it will be impossible to aim at controlling the nutritional situation that is going on in Europe, as they pretend to do so by information that has been manually obtained and processed in each country.

In the book "El libro blanco de la desnutrición clínica en España" (in Spanish) has devoted a whole chapter to thoroughly explain the design of a Computer System (fig. 7) which would be able to cover all the needs not only of Spain but also of the other European countries[52].

Early detection of undernutrition and its risk

In order to be able to detect at its origin the nutritional risk that the treated patient is suffering exposed it

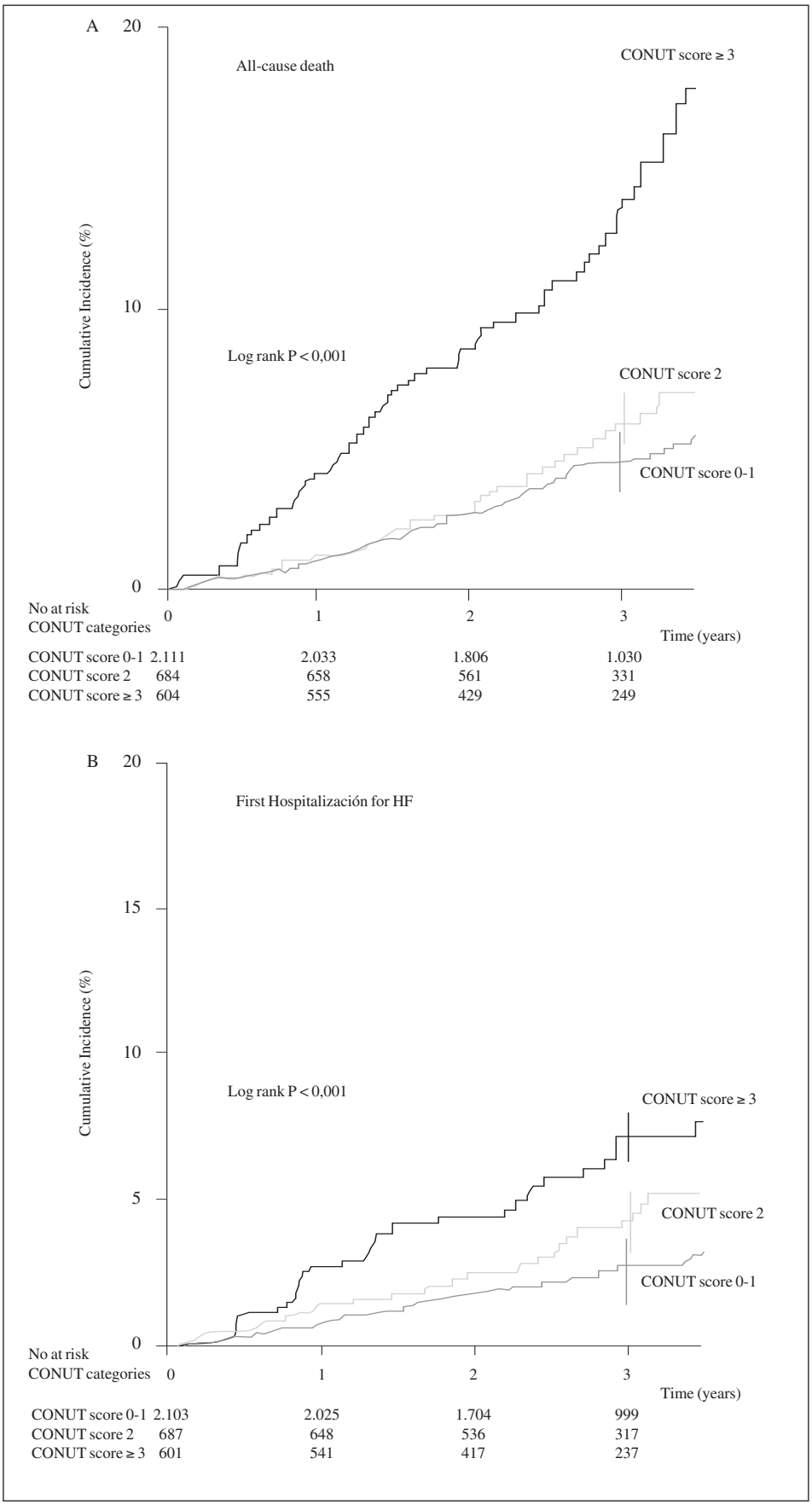

Fig. 6.—Cumulative incidence curves for (A) all-cause death and (B) first hospitalization for heart failure (HF) according to category. (Tomada de Kotaro Nochioka, MD, PhD; et al. Prognostic impact of nutritional status in asymptomatic patiens with cardiac diseases -a report from the CHART-2 Study. Circulation Journal Vol. 77, September 2013).

is essential to have access to those parameters that have proven capacity to immediately detect the frequent and acute changes which are so common during the clinical practice. Only analytical parameters can do so, and later on, after having applied the latter ones will other signs of undernutrition of be measurably by means of anthropometry or other parameters[53].

During our project we have put special emphasis in trying to focus on the very nature of the instability which is at the core of any kind of nutritional risk.

Trying to do so by placing the main attention to undernutrition as the cause did not offer many useful results that would help us see this issue with more clarity, considering that the origin of it begins with the alterations that take place in the nutritional equilibrium (trophopathy). These develop in the internal milieu as a consequence of the illness or the therapeutical procedures applied in the attempt to cure it. Our main efforts should be aimed at recovering homeostasis, which will eventually lead towards erasing any nutritional risk[40].

For many years we followed the procedures to calculate undernutrition by means of its clinical, anamnesis and anthropometrical manifestations. These parameters were useful to get a Full Nutritional Assessment (FNA), but they were of no use when trying to detect nutritional risk and its variations with due precocity. Only too late will these parameters start to give any signs of undernutrition and be in a position to calculate it properly. However, by that time the havoc has already been made, and, in fact, it could be in such an advanced state to have altered the clinical development of the patient, which could have been avoided had it been detected in due time.

We are totally convinced that the actual indicator is to be found in the nurturing area that surrounds the cell, that is, its interior milieu as coined by Claude Bernard, and which constitutes the focus where all our attention must be placed.

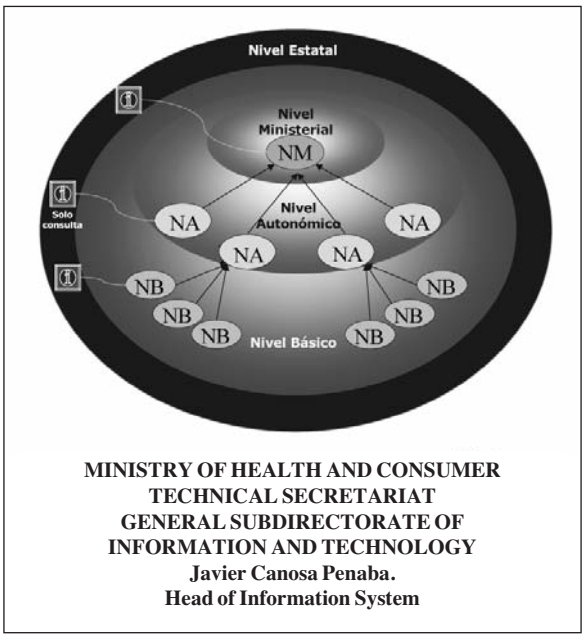

Fig. 7.—Proposal for an Information System for Early Detection of Hospital Mulnutrition.

Blood plasma is the closest possible area to it, both physically and functionally, therefore the homeostasis of this internal milieu is critical and should be maintained at all costs. It is also from that plasma that we can easily have access to the parameters which are necessary for our purposes, with the added advantage that there is a constant interchange of their content and concentration that can be traced while going on.

Applying the outdated and rudimentary manual systems indicated at present for screening in the field of early detection of Clinical Undernutrition in the treated patient is a generalized error. The need for specially trained staff and too much time which are required in this case are seldom available and, even if that was possible, those parameters would still provide poor information in the short term.

On the other hand, they require a much longer period of time in order to indicate by themselves any changes of nutritional state. They are suitable for a varied kind of studies of different size and length, but we have no evidence of being systematically applied in hospitals in the case of serious patients, with the exception of Holland. We also consider these to be discarded when aiming at the control of the fast, frequent, subtle and acute changes that can alter the nutritional equilibrium of a hospitalized patient who is further affected by aggressive treatments; those parameters will inevitably fail to achieve a weekly control of the patients at risk.

Furthermore, if we consider the technological advantages offered by the latest IT systems to our clinical practice, it is evident that we cannot but be totally in favour of integrating the automated nutritional screening tools into the already present information system for the management of clinical history data. These are highly useful to deal with analytical parameters, particularly when aiming at the follow up and control of the clinical process and nutritional support (fig. 1).

Improving the IT structures within our hospitals have played a key role in making it possible for our institutions to be in a position to incorporate automated systems for the control of CU, which have been designed by IT experts and implemented in the Clinical Information Systems already present in all Hospitals and Assisted Health Centers, as well as in the Clinical Analysis Labs. It can be said that right now we have a highly efficient method for the screening and early detection of CU as well as for the follow up of its development, which effectively integrates the data obtained by means of the analytical controls that are routinely applied to our patients.

By means of this screening procedure it is then possible to automatically collect and handle any useful data of the treated patients. This will determine the quality of the assistance received by the latter, and at the same time being able to keep that data in stock to be used eventually in epidemiological studies. This is a much easier and more effective method of getting bigger data basis as well as being practically devoid of any human mistakes due to manipulation.

Another advantage of the analytical parameters is that they are extremely useful to predict the patient's evolution, thanks to their inherent prognostic ability[54].

By means of the analytical data together and considering the initial diagnosis (or suspected diagnosis) as well as the treatments to be applied, it is possible to know a priori some key issues such as life expectancy, duration of hospital stay or the cost implied in the treatments[55].

It is important to bear in mind that the almost inexistent improvements that have been attained till the present moment in this area constitute the reason why there are 20 million people in Europe who suffer from undernutrition, as stated by the European Nutrition Health Alliance (ENHA)[56]. As a consequence it is high time to accept and opt for more modern methods which are more objective, useful, accessible, indicative, reliable, precise and ergonomic, as well as being automatically integrated in the IT systems. All these aspects make these methods much more efficient, of an unquestionable and scientifically proven validity[57,58].

Follow-up: sporadic / continuing control

Being able to detect immediately any changes caused by the illness, its treatment or the possible complications, even during the latent period in which undernutrition develops, is made possible only thanks to the application of analytical parameters. These unique tools constitute a reliable way to aim at a weekly follow up of the clinical course, as has been required by the European Council for many years.

It is also clear that a lack of nutrients caused by a deficient intake will occur in the interior milieu in the same way but at a different time. In both cases there will be a decreased concentration of the elements required for the normal functioning of the cell, that is, cell trophism.

By means of an automated method such as CONUT which is based on analytical parameters, we have been able to demonstrate that it is actually possible to detect, both automatically and at an early stage, any changes occurring in the nutritional equilibrium of the treated patient[36,60]. This has made it possible to carry out the follow ups automatically during the clinical practice (fig. 1), hence allowing us to monitor nutritional risk and treatment response with the highest precision.

This method is also an easy way to repeatedly control the clinical and nutritional evolution, therefore it offers ample possibilities reconsideration regarding the therapeutical procedures and the nutritional support as long as the results manifest and especially in the case when the latter ones may show unfavourable.

There is a well known objection to this method that is based on the possibility that "not nutritionally related" alterations may be detected by its use, which could result in false positives. However, this justification cannot be accepted considering the very nature of these types of screening systems:

- As it has been explained in relation to each of the analytical parameters that we have validated, although an alteration of these can be a consequence of the treatment, not due to nutritional deficiency, these parameters will still indicate nutritional risk. In fact, they will be indicators of undernutrition before this one appears.
- They can be integrated in the clinical control and follow up protocols, and they require practitioner's interpretation, being this the professional who will ultimately interpret the screening according to a thorough knowledge of the possible causes of the alteration
- They are easy to be repeated on a weekly basis (or even with more frequency), which means that any detected alterations will allow room for any rectifications required by an aggressive treatment, (in the case of this being the possible cause) or it will be even possible to modify the nutritional support.
- Whenever the alteration of nutritional equilibrium may persist or may become worse as indicated by the repeated clinical controls, it will become evident that undernutrition is in the process of development and that changes in the therapeutical and nutritional approaches will be necessary.

At the recovery, chronic and residential centres it is possible to suggest the same criteria as that for the control of the evolution of the hospitalized patients. This could even be applicable in the case of patients treated at home. In these cases the use of such a useful tool would definitely be of great help for the Medical Doctor, who could easily incorporate it to the existing IT Clinical system already used for the care and control of these patients. This would be facilitated considering the fact that it consists of a simple and efficient screening system for the control of undernutrition/trophopathy and the alterations related to it; it is highly possible for this condition to be already present in a vast proportion of the ill or already weak population of advanced age or particularly vulnerable conditions that are affecting their vitality.

In order to guarantee a good control of the clinical course in these cases, with the use of an automated screening system and unless any clinical changes may appear, there is no need (in the absence of an alert) to insist on the usual protocols which are intended for a full nutritional assessment (FNA).

The ageing process

Ageing is an issue that we consider requires special discussion in our field of interest, as it is clearly a rising demographic problem nowadays.

There are three main conditions behind this situation: a high prevalence of undernutrition among the elderly, an increased age of the hospitalized patients[lix] and a rising number of people residing in assistential homes and long stay centres[60-62].

These facts in addition to the higher risk involved in CU during old age[63-66] have determined the possibility of adjusting the results of the nutritional screening which we had designed for adult population in general. We tried to do so by using a correcting factor that took into account the age of the treated patient, to be applied during Phase I of CONUT, automatically issued by the IT system from the lab.

The aforementioned retrospective study[52], was carried out with 25.586 patients admitted at La Princesa Hospital of Madrid during the last couple of years. All patients who presented (at the moment of and during the first days of admittance) all the analytical data required for the nutritional screeening were included in the study.

Figures 2, 3 and 4 represent graphically how these three analytical parameters changed and the results obtained in each of the six age categories that were established among all the registered cases, starting from teenage period. In figure 5 is can be appreciated a rise of nutritional alert as a result of processing of these parameters.

As a result of this study it was concluded that it is not necessary to include the age variable because of the following reason: "Although there is strong relationship between age and undernutrition, it has been demonstrated that age does not add any information of use to the CONUT model that would improve its capacity to predict undernutrition, since the variables already used by this tool are in themselves closely linked to age. As a consequence CONUT consists of such a robust and efficient system for the prediction of undernutrition that it does not require the addition of the variable age".

This simple and retrospective study has lead us to the conclusion that through the clinical control routinely carried out in all hospitalized adult patients it is possible to obtain, in an automatical way, an efficient screening of nutritional risk, but only as long as these three parameters are included among the analysis.

That does not exclude the need of a more thorough assessment of the nutritional state in the case of a patient who is on alarm. However, the system will definitely decrease the need of carers, general costs and avoid any uncomfort suffered by the patients as a consequence of being routinely manipulated for exploration and anamnesis purposes.

Considering the ageing process and going back to the issue of the use of albumin as a nutritional marker, it is normally said that "in the elderly patient (hipoalbuminemia) can be linked to the mere presence of sarcopenia". We agree with this and in fact it is precisely due to this reason why we have selected these parameters as indicators of a diminished functional capability in the body, as well as markers of risks, because sarcopenia is absolutely involved in the ageing process, that is, it is an inherent aspect of it. Furthermore, considering that this loss is related to involutive changes that take place during ageing, these analytical parameters play a key role as they progressively change over time, and this is closely linked with a diminished activity of the cells (figs. 2 y 4).

One of the main reasons for insisting on these points (which are in opposition to the officially established concepts at present) is the consensus declaration issued by both Societies, SENPE and SEGG[10]. The prologue to this consensus mentions the possibility making periodic revisions of the criteria contained in it. This has made us think it is high time to suggest that an update of it should be done, at least rearging this issue, and we consider it would be reasonable to devote more credit and give priority to the use of analytical parameters for nutritional screening methods.

Nutritional prognosis

This is another advantage offered by the screening tools, especially the ones based on analytical parameters and which have become more widely used in the last years[67-70]. We are not planning to devote much attention to this in the present study; this it will be eventually done by future research.

We would like however to highlight the acknowledged prognostic capacity offered by the screening tools which are based on analytical parameters such as plasmatic albumin concentration and total cholesterol and lymphocyte count[56,71,72], all of which make these tools even more useful at the moment of planning with due time any decisions to be taken towards treating the patient. Being aware of a patient's nutritional risk in different pathological conditions facilitates the decision taking process by allowing a better selection of certain therapeutical procedures in favour of alternative ones (medicine, transplants, surgery, etc.)[71,73-74].

In order to know the proven risks implied by each pathological process and the therapeutical procedures, it will be necessary to make reference to BIG DATA. This makes use of the data generated in the clinical practice and analyses the final clinical results obtained through a variety of therapeutical procedures according to each clinical process. By means of this it is possible to collect a sufficient amount of data which will be highly useful to predict the prognosis associated to each process, both of this in itself as well as in accordance with the treatment applied, therefore this will determine a higher possibility of making the best decision.

A proper validation of a screening tool is not guaranteed by making reference to the nutritional state assessment (as done till now) carried by any of the possible procedures of different certainty but, rather, by direct application in order to confirm the assessment issued by the initial screenings, and then comparing these with the final results, once the clinical process has been finished.

This entails a key objective to achieve by means of the new technology available for the management of big data bases. It would imply the end of a process which was originally designed at the end of the last century, and which we trust will soon become a reality thanks to the advances in the information systems of our hospital settings and other health centres. The latter ones will be in a position to offer a better assistential quality to the ill and vulnerable patients[75,76].

Comparison of different screening systems

We have been able to prove through the latest revisions that the use of these parameters are much more specific and sensitive than most of the other screening systems that are used these days[77]. In this regard it is particularly indicative the comparative table published by U. Kyle in July 2006[78], where the statistical results obtained by NRI, MUST and NRS-2002 are compared with those obtained by SGA as gold standard. The same results were added, as obtained by Phase 1 of CONUT automatic nutritional screening tool (table I).

Table I
Statistical comparison of the nutritional assessment with SGA versus the values of several tools screening at hospital admission: NRI, MUST, NRS-2002 and CONUT

Name (n =)	*NRI (237)*	*MUST (995)*	*NRS-2002 (995)*	*CONUT-1 (161)*
Sensitivity	43.1	61.2	62.0	78.26
Specificity	89.3	78.6	93.1	89.13
Prognoastic value positive	76.2	64.6	85.1	84.38
Prognostic value negative	66.3	76.1	79.4	84.54
Kappa Index	0.24	0.26	0.48	0.68

Modified from Ursula G. Kyle et al. *Clinical Nutrition* 2006; 25 (3): 409-17.

A comparison of the three systems studied by Kyle with our own system indicates that CONUT is obviously much better at predicting the statistical data, an exception of this being the sensitivity demonstrated by NRS-2002, but only of 3.97 % difference.

It is important to mention that the SGA, frequently used as the gold standard for undernutrition, is based in some parameters that are more similar to the ones used by NR-S2002 than by CONUT. Both tools have the same approach, that is, they are aimed at searching for primary undernutrition rather than clinical trophopathy. On the other hand, CONUT is able to anticipate and detect any possible risk in due time, even in cases where the other systems have not even been able to detect undernutrition.

Conclusions

Nutritional screening systems are aimed at people who are in a situation of or at risk of suffering an alteration in their nutritional state (that is to say, not necessarily for people who are already undernourished), with the purpose of taking the necessary measures in due time.

The manual screening tools which are recommended at present have the search for undernutrition as their objective. They should be considered as miniatures of undernutrition diagnosis systems and they can only aim at detecting the condition once the risk is well established, hence taking too long in the clinical practice. They are slower as well as more complex, expensive and imprecise, apart from having too many subjective appreciations.

On the other hand, when a method is based on analytical parameters they are able to detect any changes automatically and to measure directly among the cell environment, so they are very efficient to value (through quantity or persistence) any possibilities that the condition may become worse. A record of this information is part of the clinical data which is routinely applied for the clinical control of the patient.

As a general summary these screening systems have proven highly efficient because of the following:

1. They are based on rigorous scientific arguments.
2. They are more sensitive to detect the frequent changes of the nutritional equilibrium in the hospitalized and treated patient.
3. They detect any nutritional alteration during its period of latency, hence anticipating to the anatomical manifestations that indicate undernutrition.
4. They are more efficient and easy to apply even automatically, which makes them more objective, efficient and easier to reproduce.
5. They can be directly included in the protocols for the control of the clinical situation of our patients, playing a key role in improving assistential quality.
6. They do not require much time or additional resources to get more specific anamnesis and anthropometric data.
7. They are not a cause of uncomfort to the patients.
8. They facilitate the decision taking process by means of giving a priori information regarding possible risks.
9. They are available at hospitals, day-care centres, residencies or in home settings, while they do not imply additional protocols, costs or professional dedication.
10. They fully comply with all the requirements for screening methods established by European Council recommendations of 2003[17].

By adopting the modern screening methods, as those based on analytical parameters, it is possible to achieve great improvements in the field of nutritional control of the vulnerable and elderly patients under our care; these methods would be key in being able to offer a better assistential quality and results, as well as to prevent eventual complications and reduce costs.

All the above shows that it is high time to suggest the whole Society (and those entities involved in consensus agreements) that a revision of the screening and nutritional control procedures should be done in order to update the established protocols. We consider there is enough reason to justify this initiative, and by doing so it would imply a totally different approach to the issue of Clinical Undernutrition, being an opportunity for our more modern and efficient system to be offered abroad[33b,53] (fig. 7).

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